

WHAT IS CLAIMED IS:

1. An isolated polypeptide encoding a DFF40 DNA fragmentation factor.
- 5 2. The polypeptide of claim 1, wherein the DNA fragmentation factor has the amino acid sequence as set forth in SEQ ID NO:2.
3. An isolated peptide having between about 10 and about 50 consecutive residues of a DFF40 DNA fragmentation factor.
- 10 4. The peptide of claim 3, wherein the peptide is conjugated to a carrier molecule.
5. The peptide of claim 4, wherein the carrier molecule is selected from the group consisting of KLH and BSA.
- 15 6. The peptide of claim 4, wherein the DNA fragmentation factor has an amino acid sequence of about 10 to about 50 consecutive residues of SEQ ID NO:2.
7. A monoclonal antibody that binds immunologically to a DFF40 DNA fragmentation factor.
- 20 8. The monoclonal antibody of claim 7, wherein the antibody does not bind immunologically to other human polypeptides.
- 25 9. The monoclonal antibody of claim 7, wherein the antibody further comprises a detectable label.
10. The monoclonal antibody of claim 9, wherein the label is selected from the group consisting of a fluorescent label, a chemiluminescent label, a radiolabel and an enzyme.
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11. A hybridoma cell that produces a monoclonal antibody that binds immunologically to a DFF40 DNA fragmentation factor.
12. The hybridoma cell of claim 11, wherein the antibody does not bind immunologically to other human polypeptides.
13. A polyclonal antisera, antibodies of which bind immunologically to a DFF40 DNA fragmentation factor.
14. The antisera of claim 13, wherein said antisera is derived from an animal other than a human.
15. An isolated nucleic acid comprising a region, or the complement thereof, encoding a DFF40 DNA fragmentation factor or an allelic variant thereof.
16. The nucleic acid of claim 15, wherein the DFF40 DNA fragmentation factor is human.
17. The nucleic acid of claim 16, wherein said DNA fragmentation factor has the amino acid sequence of SEQ ID NO:2.
18. The nucleic acid of claim 17, wherein said nucleic acid sequence comprises the coding region having the sequence of SEQ ID NO:1 or the complement thereof.
19. The nucleic acid of claim 15, wherein said nucleic acid is selected from the group consisting of genomic DNA, complementary DNA and RNA.

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49. The method of claim 47, wherein said DFF40 is provided as a protein complex comprising a DFF45 DNA fragmentation factor, and further comprising causing said DFF45 to be cleaved.

50. The method of claim 49, wherein the cleavage is effected by increasing the activity of caspase 3.

51. The method of claim 47, wherein said providing comprises contacting said cell with a first expression construct comprising a first nucleic acid encoding a DFF40 polypeptide and a promoter functional in eukaryotic cells wherein said first nucleic acid is under the control of said promoter.

52. The method of claim 47, further comprises providing a factor selected from the group consisting of a histone, a high mobility group protein and a nuclear factor.

53. The method of claim 51, wherein said expression construct comprises a viral vector.

54. The method of claim 51, wherein said viral vector is selected from the group consisting of retrovirus, adenovirus, vaccinia virus, herpesvirus and adeno-associated virus.

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71. The method of claim 70, wherein the cleavage is effected by increasing the activity of caspase 3.
72. The method of claim 65, wherein said providing comprises contacting said cell with a first expression construct comprising a first nucleic acid encoding a DFF40 polypeptide and a promoter functional in eukaryotic cells wherein said first nucleic acid is under the control of said promoter.
73. The method of claim 72, wherein said expression construct further comprises a second nucleic acid encoding a DFF45 polypeptide, and wherein said DFF45 is altered, with respect to wild-type DFF45, such that it lacks anti-apoptotic function but retains DFF40-chaperone function.
74. The method of claim 73, wherein said expression construct further comprises an internal ribosome entry site (IRES), wherein said IRES is positioned 3' to the upstream nucleic acid and 5' to the downstream nucleic acid.
75. The method of claim 73, wherein said expression construct further comprises a second promoter functional in eukaryotic cells, wherein said second nucleic acid is under the control of said second promoter.
76. A method for treating cancer comprising the step of contacting a tumor cell within a subject with a nucleic acid (i) encoding a DFF40 DNA fragmentation factor and (ii) a promoter active in said tumor cell, wherein said promoter is operably linked to the region encoding said DNA fragmentation factor, under conditions permitting the uptake of said nucleic acid by said tumor cell.
77. A method of identifying a modulator of DFF40 activity comprising the steps of:
 - (i) providing a cell expressing a DFF40/DFF45 complex;

- (ii) contacting said cell with a candidate substance;
- (iii) activating DFF40; and
- (iv) comparing the apoptosis of the cell in step (iii) with the apoptosis observed when said candidate substance is not added,

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wherein an alteration in apoptosis indicates that said candidate substance is a modulator said apoptotic activity.

78. The method of claim 77, wherein said cell is a tumor cell.

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79. The method of claim 77, wherein said apoptosis is measured using a parameter selected from the group consisting of DNA fragmentation, DNA condensation, DFF40 expression, nuclease activation, caspase activation, and DFF cleavage.

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80. The method of claim 77, wherein said candidate substance is a chemotherapeutic or radiotherapeutic agent.

81. The method of claim 77, wherein said candidate substance is selected from a small molecule library.

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82. The method of claim 77, wherein said candidate substance is a protein.

83. The method of claim 77, wherein said candidate substance is a DFF45 analogue.

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84. The method of claim 77, wherein said candidate substance is a high mobility group (HMG) protein analogue.

85. The method of claim 84, wherein said HMG protein is HMG-1.

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86. The method of claim 84, wherein said HMG protein is HMG-2.

87. The method of claim 84, wherein said HMG protein is HMG-14.
88. The method of claim 77, wherein said candidate substance is a nuclear factor.
89. The method of claim 88, wherein said protein is an histone.
90. A modulator of apoptotic activity identified according to a method comprising the steps of:
- (i) providing a cell expressing a DFF40/DFF45 complex;
 - (ii) contacting said cell with a candidate substance;
 - (iii) activating DFF40; and
 - (iv) comparing the apoptosis of the cell in step (iii) with the apoptosis observed when said candidate substance is not added,
- wherein an alteration in apoptosis indicates that said candidate substance is a modulator said apoptotic activity.
91. An isolated DNA fragmentation factor complex for regulating chromatin stability, said complex comprising a DFF40 polypeptide and a DFF45 polypeptide.
92. The complex of claim 91, wherein said DFF40 subunit has the sequence of as set forth in SEQ ID NO:2.
93. The complex of claim 81, wherein said DFF45 subunit has the sequence of as set forth in SEQ ID NO:4.
94. A method of producing a functional DNA fragmentation factor comprising:

- (i) providing to a cell
 - (a) a first nucleic acid encoding a DFF40 polypeptide; and
 - (b) a second nucleic acid encoding a DFF45 polypeptide; and
- (ii) expressing said complex in a cell,

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wherein the coexpression of said polypeptides allows for the formation of a functional DFF40 polypeptide.

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95. The method of claim 94, further comprising the step of causing said DFF45 polypeptide to be cleaved by caspase 3.

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96. The method of claim 94, wherein said first and said second nucleic acids are contained in the same expression construct and both are under the control a first promoter.

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97. The method of claim 96, where said expression construct further comprises an internal ribosome entry site (IRES) positioned 3' to the upstream gene and 5' to the downstream gene.

98. The method of claim 94, wherein said first and said second nucleic acids are contained in the same expression construct and are under the control a first and a second promoter, respectively.

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99. The method claim 94, wherein said first and said second nucleic acids are contained in different expression constructs and are under the control a first and a second promoter, respectively.

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100. The method of claim 94, wherein said second nucleic acid encodes a DFF45 polypeptide that is altered, with respect to wild-type DFF45, such that it lacks anti-apoptotic function but retains DFF40-chaperone function.